REMARKS/ARGUMENTS

Reconsideration of the present application, as amended, is respectfully requested.

A. STATUS OF THE CLAIMS

As a result of the present amendment, claims 21, 30-31, 35-36, and 39-40, and new claims 48-55 are presented in the case for continued prosecution.

Claim 21 has been amended to further describe the claimed binding domains and functional group domain. Support for the amendment can be found, for example, in cancelled claim 27.

Claim 21 has also been amended to address issues raised by the Examiner with respect to novelty requirement. The claim, as amended herein, specifies the location of one of the uncoupled cysteines. Support can be found, for example, in Example 6 found on pages 66-70, particularly on page 66, lines 21-23 and Table 11 on page 69. See also pages 31-44 (Table 4 on page 40).

Claims 22-29 have been cancelled without prejudice.

Claims 30-31 have been amended to remove multiple dependencies and conform to US patent practice.

Claims 32-34 have been cancelled without prejudice.

Claim 35 and 39-40 have been amended to remove multiple dependencies and conform to US patent practice.

Withdrawn claims 37, 41-43 and 46-47 have been amended to removed multiple dependencies and conform to US patent practice. Withdrawn claim 43 has also been amended to specify the extension peptide corresponding to claim 31 (thus, claim 21), as amended herein.

New claims 48-49 have been added to specify the number of uncoupled cysteines. Support can be found, for example, in Example 4 found on pages 56-65 of the specification.

New claims 50-52 have been added to include specific extension peptides. Support can be found, for example, in cancelled claims 24-26, respectively.

New claims 53-54 have been added to include specific functional group domains. Support can be found, for example, in cancelled claims 28-29 and on page 25, lines 6-11 and page 43, line 12-14.

New claim 55 has been added to include a specific extension peptide. Support can be

found, for example, on page 39, line 21.

It is believed that new claims 48-55 are drawn to the elected invention, Group 1, and read on the elected species. No new matter has been added.

B. CLAIM OBJECTIONS

On page 4 of the Office Action, claims 27, 30-31, 35-36 and 39-40 are objected to as being improper dependent claims. In response, multiple dependencies have been removed from the claims and the claims objected to have been amended to depend from claim 21, rendering the objections moot. Claim 27 has been cancelled without prejudice.

C. CLAIM REJECTIONS UNDER 35 USC §112, FIRST PARAGRAPH

On pages 4-6 of the Office Action, claims 21, 30-31, 35-36, and 39-40, are rejected under 35 USC 112, first paragraph, as allegedly failing to comply with the written description requirement.

In the last paragraph on page 4 of the Office Action, the Examiner indicated that "the binding domain cannot be any molecule that binds to any other molecule, i.e., any antibody, any ligand or any receptor but must be an antibody, ligand or receptor that binds to a cell-surface antigen". Emphasis added. The Examiner further indicated that the specification does not provide guidance for the functional group domain.

In response thereto, claim 21 has been amended to adopt a scope which is believed to be commensurate with what the Examiner has indicated is proper. Claim 21, as amended herein, specifies that the binding domain is an antibody, a ligand or a receptor that binds to a cell-surface antigen, and the functional domain is an enzyme.

The recombinant fusion protein monomer contemplated in the present application includes molecules such as enzymes, proteins, drugs, biosensors, etc as the functional group domain. Referring to peer-reviewed articles such as Hudson, P.J., *Curr. Opin. Immunol.*, 1999, 11:548-555, and Bagshawe, K.D., et al., *Curr. Opin. Immunol.*, 1999, 11:579-583, the specification described that molecules other than enzymes or proteins such as drugs can be conjugated to form a fusion protein. See also George T. et al., *Methods in Molecular Medicine: Diagnostic and Therapeutic Antibodies*, Human Press, New Jersey, USA, 2000. Thus, those of ordinary skill in the art can make the recombinant fusion protein containing molecules other than

enzyme (protein) as a functional group domain without undue experimentation according to the disclosure in the specification and the knowledge known in the art.

As such, the amendments to the claims have been made in an effort to expedite the prosecution of the present application rather than to indicate that the rejections made by the Examiner are accepted, or as an admission of the soundness of the rejections made by the Examiner.

Applicants specifically reserve the right to file one or more continuation applications to prosecute the subject matter removed from the claims.

Accordingly, reconsideration and withdrawal of the rejections under 35 USC 112, first paragraph, is respectfully requested.

D. CLAIM REJECTIONS UNDER 35 USC §112, SECOND PARAGRAPH

On pages 6-7 of the Office Action, claims 21, 30-31, 35-36, and 39-40, are rejected under 35 USC 112, second paragraph, as allegedly being indefinite. Briefly stated, the Examiner indicated that the claims are indefinite because claim 27 includes elements (non-protein molecules) which do not conform to the preamble of claim 21. The Examiner also indicated that the recitation "one of the binding domain is an antibody" in claim 35 is ambiguous. The Examiner required the claims to be rewritten in standard U.S. English.

As amended herein, claim 21 recites that the functional group domain is an enzyme (protein). As requested by the Examiner, the claims have been amended to conform to U.S. patent practice.

In view of the above, the claims are definite. Reconsideration and withdrawal of the rejections under 35 USC 112, second paragraph, is respectfully requested.

E. REJECTIONS UNDER 35 U.S.C. §102(b)

The Examiner has rejected the subject matter of claims 21, 30-31, 35-36, and 39-40 under 35 U.S.C. 102(b) as allegedly being anticipated by Choi et al. (Bull. Korean Chem. Soc., 2001, 22:1361-1365) as evidenced by Ogata et al. (J. Biol. Chem., 1990, 265:20678-20685). The Examiner has taken the position that Choi et al. teaches fusion protein monomers and dimers which can be encompassed by the rejected claims.

Claims 21, 30, 35-36, and 39 are rejected under 35 USC 102 (b) as allegedly being

anticipated by Behringwerke AG (EP 501215A2). According to the Examiner, a fusion protein monomer of Behringwerke can be encompassed by the rejected claims.

A rejection under 35 U.S.C. 102(b) requires that all of the elements of the rejected claims be found within the cited reference. Claim 21 and its dependent claims, as amended herein, require that at least one of the uncoupled cysteines of the extension peptide is located at the fourth amino acid position from the binding domain.

The fusion protein monomers of Choi et al. include an uncoupled cysteine at the first amino acid position from the binding domain. The fusion protein monomers of Behringwerke AG include an uncoupled amino acid at the fifth position from the binding domain.

"Uncoupled cysteine" refers to a cysteine that does not have its matching cysteine to form a disulfide bond within the monomer. For example, cysteines in VH, CH1, VL and CL domains forming intra-domain disulfide bonds in a Fab fragment of an antibody are not uncoupled cysteines. Uncoupled cysteines in the extension peptide of the claimed invention are able to form a disulfide bond bridge between two monomers and provide a dimer.

Applicants respectfully draw the Examiner's attention to the fact that the fusion protein monomer including an uncoupled cysteine positioned at the fourth amino acid from the binding domain significantly enhanced the dimer formation compared to the fusion protein monomer including an uncoupled cysteine positioned at the first amino acid from the binding domain as in Choi et al. Such data is set forth, for example, in Table 11 found on page 69 of the specification. The claimed fusion protein monomers containing an uncoupled cysteine at position 4 and multiple flexible amino acids (e.g., the number of GASQEND is 6, 11, 16, 21, etc.) showed more than 10 fold dimer formation compared to that of Choi (fusion protein monomer and dimmers prepared by pCE1 of Table 11 correspond to those of Choi et al.).

Without being bound by any theory, the improved refolding and dimer formation of the claimed invention is attributed in part to the fact that undesired disulfide scrambling chain reaction is significantly decreased. On the other hand, it is believed that the uncoupled cysteine (at position 1) of Choi et al. is located very close to coupled cysteines within the binding domain and interferes the intradomain and interdomain disulfide bond formation between the coupled cysteines.

Thus, it is respectfully urged that claims 21, 30-31, 35-36, and 39-40 and new claims 48-54 are not anticipated by either Choi et al. or Behringwerke AG. For all of the above reasons,

reconsideration and withdrawal of the rejections is respectfully requested.

F. REJOINDER

The withdrawn claims have been amended to adopt the limitations of claim 21. Thus, if claim 21 is allowed, Applicants request rejoinder of the claims directed to the subject matter removed by the Examiner.

G. FEES

This response is being filed with a petition for a three-month extension of time and the required fee via credit card authorization. November 27, 2008 was a federal holiday, Thanksgiving Day. Therefore, this response is timely.

No further fee is believed to be required. If, on the other hand, it is determined that any further fees are due or any overpayment has been made, the Assistant Commissioner is hereby authorized to debit or credit such sum to deposit account 02-2275. Pursuant to 37 C.F.R. 1.136(a)(3), please treat this and any concurrent or future reply in this application that requires a petition for an extension of time for its timely submission as incorporating a petition for extension of time for the appropriate length of time. The fee associated therewith is to be charged to Deposit Account No. 02-2275.

H. CONCLUSION

In view of the actions taken and arguments presented, it is respectfully submitted that each and every one of the matters raised by the Examiner have been addressed by the present amendment and that the present application is now in condition for allowance.

An early and favorable action on the merits is earnestly solicited.

Respectfully submitted,

LUCAS & MERCANTI, LLP

By: /Michael N. Mercanti/
Michael N. Mercanti
Registration No. 33,966

Hyun Soon Cho

LUCAS & MERCANTI, LLP
475 Park Avenue South
New York, New York 10016
Phone: 212-661-8000
Fax: 212-661-8002